

Serial No.: 09/645,456

Filing Date: 24 August 2000

31. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves assaying cytokinesis.

### REMARKS

Claims 19-31 are pending. Following from a phone interview between Robin Silva and Examiner Landsman on November 4, 2002, Claims 20 and 22 have been amended to remove the term "about" from the phrase "at least about". Further, Claim 22 has been amended to recite assays for determining the effect of a candidate bioactive agent. Support for amended Claim 22 is found in the specification, for example, at page 38, lines 20-24. Claims 26-31 depend from Claim 22. Support for new claims 26-31 is found in the specification, for example, at page 38, lines 20-24.

The current amendment also corrects the instant specification, denominating the instant application a divisional of U.S. Serial No. 09/425,324 filed October 21, 1999.

Attached hereto is a sheet titled, "Version With Markings to Show Changes Made" which depicts the changes made to the instant application by the current amendment.

### CONCLUSION

Applicant submits that the application is now in condition for allowance, and early notification of such is requested. If there remain issues that the Examiner believes may be resolved by telephone, he/she is respectfully requested to contact the undersigned at (415) 781-1989.

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Respectfully submitted,  
DORSEY & WHITNEY LLP

Date: 11/4/02

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In the Specification:

At page 1, line 9:

This application is a divisional of U.S. Serial No. 09/425,324 filed October 21, 1999 [~~09/645,793 filed 24 August 2000~~]. The present invention is directed to compositions involved in cell cycle regulation and methods of use. More particularly, the present invention is directed to genes encoding proteins and proteins involved in cell cycle regulation. Methods of use include use in assays screening for modulators of the cell cycle and use as therapeutics.

At page 12, line 14:

Another example of a useful algorithm is the BLAST algorithm, described in Altschul, et al., J. Mol. Biol., 215:403-410, (1990) and Karlin, et al., PNAS USA, 90:5873-5787 (1993). A particularly useful BLAST program is the WU-BLAST-2 program which was obtained from Altschul, et al., Methods in Enzymology, 266:460-480 (1996); [~~http://blast.wustl.edu/blast/README.html~~]]. WU-BLAST-2 uses several search parameters, most of which are set to the default values. The adjustable parameters are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11. The HSP S and HSP S2 parameters are dynamic values and are established by the program itself depending upon the composition of the particular sequence and composition of the particular database against which the sequence of interest is being searched; however, the values may be adjusted to increase sensitivity.

In the Claims:

20. (twice amended) A method of screening for a bioactive agent capable of interfering with the binding of a TNF protein and a Traf2 or Nck protein, said method comprising:

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a) combining a TNF protein, a candidate bioactive agent, and a Traf2 or Nck protein;  
and  
b) determining the binding of said TNF protein to said Traf2 or Nck protein;  
wherein said TNF protein comprises an amino acid sequence having at least [about] 95% identity to SEQ ID NO:34, and wherein said TNF protein will bind to said Traf2 or Nck protein in the absence of said candidate bioactive agent.

22. (twice amended) A method of screening for a bioactive agent capable of modulating the activity of a TNF protein, said method comprising:

a) adding a candidate bioactive agent to a cell comprising a recombinant nucleic acid encoding a TNF protein; and  
b) determining the effect of said candidate bioactive agent on said cell;  
wherein said TNF protein comprises an amino acid sequence having at least [about] 95% identity to SEQ ID NO:34, [and] wherein said TNF protein will bind to Traf2 or Nck, and wherein determining the effect of said candidate bioactive agent on said cell involves assaying at least one parameter selected from the group consisting of Nck activity, Traf2 activity, JNK pathway activity, F-actin disruption, cell spreading, phosphorylation of Gelsolin, mitosis, and cytokinesis.

24. The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves [measuring] assaying JNK pathway activation in said cell.

25. The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves [observing actin filament rearrangement] assaying F-actin disruption in said cell.

26. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves assaying Nck activity.

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27. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves assaying Traf2 activity.
28. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves assaying cell spreading.
29. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves assaying phosphorylation of Gelsolin
30. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves assaying mitosis.
31. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves assaying cytokinesis.